IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

PATENT

Applicants: Janus, et al.

Serial No: 09/923,616

Filed: August 6, 2001

Title: METHODS OF TREATING CANCER AND THE PAIN ASSOCIATED THEREWITH USING ENDOTHELIN ANTAGONISTS

Case No.: 6715.US.02

Group Art No.: 1614

Examiner: (not yet assigned)

I hereby certify that this paper (along with any paper referred to as being attached or enclosed) is being deposited with the United States Postal Service on the date shown below with sufficient postage as first class mail in an envelope addressed to the:

Assistant Commissioner for Patents
Washington, D.C. 20231, on:

Date of Deposit: November 15, 2001

Tanya Parent 11/15/01
Tanya Parent Date

Assistant Commissioner for Patents
Washington, D.C. 20231

Dear Sir:

INFORMATION DISCLOSURE STATEMENT

Pursuant to 37 C.F.R. §§ 1.56 and 1.97(b), Applicants bring to the attention of the Examiner the documents listed on the attached PTO 1449. This Information Disclosure Statement is being filed, to the knowledge of the undersigned, before the mailing date of a first Office Action on the merits. Applicants respectfully petition and request that the Examiner consider the listed documents and evidence such consideration by making appropriate notations on the attached form. Copies of the listed documents are attached.

Applicants further reserve the right to take appropriate action to establish the patentability of the disclosed invention over the listed documents, should one or more of the documents be applied against the claims of the present application.

The Commissioner is authorized to charge our Deposit Account any additional fees (or credit any over payments) that may be required under 37 C.F.R. §§ 1.16 and 1.17 in association with this communication for which full payment has not been tendered.

Respectfully submitted,
T. Janus, et al.

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OTHER DOCUMENTS (Including Author, Title, Date, Place of Publication)

	C1	Bang-Lun et al. Synthesis and Anticholinergic Activity of Some Derivatives of Substituted Glycolates, Acta Pharmaceutica Sinica 1985:: 20 (6), pp. 427-432
	C2	Bhagwat, Synthésis of Enantiomerically Pure Pyrrolidinones as Endothelin Receptor Antagonists Tetrahedron Letters, Vol 37, No 27, pp 4627-4630, 1996
	C3	Buyukgebiz, BQ-123, a specific endothelin (ET_A) receptor antagonist, prevents ischemia-reperfusion injury in kidney transplantation. Transplant Int 1996, 9, 201-207
	C4	Clozel et al. Pathophysiological role of endothelin revealed by the first orally active endothelin receptor antagonist. Nature 365 : 759-761 (1993)
	C5	Craig et al., Drug Absorption and Distribution. Modern Pharmacology pp 33-35
	C6	Ferro et al. The Clinical Potential of Endothelin Receptor Antagonists in Cardiovascular Medicine. Drugs, Volume 51 Issue: page 12 – 27 (1996)
	C7	Hogaboam et al. An orally active non-selective endothelin receptor antagonist, bosentan, markedly reduces injury in a rat model of colitis. European Journal of Pharmacology 309 (1996) pp 261-269
	C8	Itoh et al. A Novel Endothelin ET ReceptorAntagonist, BQ-485, and Its Preventive Effect On Experimental Cerebral Vasospasm In Dogs. Biochem. Biophys. Res. Comm. 195: 969-975 (1993)
	C9	Itoh et al. Cloning and sequence analysis of cDNA encoding the precursor of a human endothelium-derived vasoconstrictor peptide, endothelin: identity of human and porcine endothelin. FEBS LETTERS, April 1988 Volume 231, number 2, pp 440-444
	C10	Jae it al. Pyrrolidine-3-carboxylic Acids as Endothelin Antagonists. J. Med. Chem. 1997, 40. 3217-3227
	C11	Nelson et al. Identification of endothelin-1 in the pathophysiology of metastatic adenocar4cinoma of the prostate. Nature Medicine 1995, 1, 944-949
	C12	Nelson et al. New Bone Formation in an Osteoblastic Tumor Model is Increased By Endothelin-1 Overexpression and Decreased by Endothelin A Receptor Blockade. Urology 53: 1063-1069, 1999
	C13	Rahman, Synthesis of 4-Substituted Thiosemicarbazones of 3-Methyl-4-phenylpyridine-2carboxaldehyde as Anti-tumor Agents. Indian J. Chem., Vol. 19B, September 1980,
	C14	Seydal et al. Absorption, Distribution, and Metabolism of Drugs. Quantitative Structure-Activity Relationships of Drugs (1983) (German Translation behind)
	C15	Tasker et al. Potent and Selective Non-Benzodioxole-Containing Endothelin-A Receptor Antagonists. J. Med. Chem. 1997, 40. 322-330
	C16	Tsuge, et al. Synthetic Versatility of N-(Silylmethyl)imines :Water-Induced Generation of N-Protonated Azomethine Ylides of Nonstabilized Type and Floride Induced Generation of 2-Azaallyl Anions. Bull. Chem. Soc. Jpn., 59, 2537-2545 (1986)
	C17	Tsuge et al. Water-Induced Formation of Azomethine Ylide 1, 3-Dipole. Stereospecific and Regioselective Cycloaddition Reactions. Chemistry Letters, pp 801-804 (1984)
	C18	Watanabe et al. Endothelin in myocardial infarction. Nature- London 344 p 114 (1990)
	C19	Winn et al. Diarylpyrrolidine-3-carboxylic Acids- Potent Eta Selective Endothilin Receptor Antagonists. J. Med. Chem. 1996,39, pp 1039-1048
	C20	Chemical Abstracts Vol 74, 1971 p 304
	C21	27-Heterocycles Vol. 119, 1993 p 999
	C22	Yanagisawa et al. A novel potent vasoconstrictor peptide produced by vascular endothelial cells. Nature 332 411- 415 (1990)
	C23	Kon, et al., Glomerular Actions of Endothelin in Vivo", J. Clin. Invest. 83 1762 - 1787 (1989)
	C24	Kon, "Role of Endothelin in Cyclosporine-induced Glomerular Dysfunction", Kidney Int. 37 1487 - 1491 (1990)

EXAMINER | **DATE CONSIDERED**

EXAMINER: Initial citation considered. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

(Form PTO 1449)

DATE: 11/15/01 SHEET 1 of 2

Form PTO - 1449 (Modified)

FORM PTO-1449 (Modified) U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE	ATTY. DOCKET NO. 6715.US.O2	SERIAL NO. 09/923,616
INFORMATION DISCLOSURE STATEMENT BY APPLICANT	APPLICANT(S) Janus et al.	
(Use several sheets if necessary)	FILING DATE August 6, 2001	GROUP
(37 CFR 1.98 (b))		

U.S.PATENT DOCUMENTS

EXAMINER INITIAL		PATENT NUMBER	ISSUE DATE	INVENTOR	CLASS	SUB CLASS	FILING DATE
	A1	3,342,833	9/19/67	Fremery			
	A2	4,132,709	2/2/79	Santroch et al.			
	A3	4,216,218	8/5/80	Klioze et al.			
	A4	4,340,715	7/20/82	Grounder et al.			
	A5	5,482,960	1/9/96	Berryman et al.			
	A6	5,668,164	9/16/97	Ma et al.			

FOREIGN PATENT OR PUBLISHED FOREIGN PATENT APPLICATION

		DOCUMENT NUMBER	PUBLIC-ATION DATE	COUNTRY OR PATENT OFFICE	CLASS	SUB CLASS	TRANS-LATION YES	TRANS-LATION NO
	B1	0 439 444 A2	31.07.91	EP				
	B2	2 275 926 A	14.09.94	UK				
	B3	93/08799	13.05.93	PCT				
	B4	94/02474	03.02.94	PCT				
	B5	94/14434	7.07.94	PCT				
	B6	95/04534	16.02.95	PCT				
	B7	95/05372-A1	09.08.94	PCT				
	B8	95/05376	23.02.95	PCT				
	B9	95/33748	14.12.95	PCT				
	B10	95/33752	14.12.95	PCT				
	B11	95/35107	28.12.95	PCT				
	B12	96/06095	29.02.96	PCT				
	B13	97/30046	21.08.97	PCT				

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